REMARKS

Claims 1-46 were pending in the application. Claims 1-46 were rejected. Claims 1-46 are canceled without prejudice to or disclaimer of the subject matter recited therein. Claims 47-81 are added. Claims 47-81 are now pending in the application. Claims 47, 62, and 67 are the independent claims. Reconsideration of the amended application is respectfully requested.

The examiner objected to the drawings because of a German-language label in Figure 2. A corrected drawing sheet is submitted herewith in compliance with 37 CFR 1.121(d). The objection, therefore, should be withdrawn.

The examiner objected to the disclosure because of certain noted informalities. The written description is amended to correct the noted informalities. The objection, therefore, should be withdrawn.

The examiner objected to claims 1, 2, 15, 16, 21, 29, 32, 40, and 44 due to certain noted informalities. These claims are canceled. The objection, therefore, should be withdrawn.

The examiner rejected claims 11, 28, 33, and 45 under 35 USC §112, first paragraph as failing to comply with the enablement requirement. These claims are canceled.

Claims 11 and 28 correspond to the subject matter recited in new claim 57. Claim 57 recites ribs having a height in a range of 1 nm to 10 nm. This range falls within the range disclosed in the written description, for example, on page 5, at lines 14-15. As disclosed in the written description in the paragraph beginning on page 13, at line 25, ribs

of this height can be fabricated using, for example, a silicon wafer cut in the (111) plane and edged with KOH as the die.

Claims 33 and 45 correspond to the subject matter recited in new claim 67. The Examiner stated that insufficient explanation is given in the specification regarding how electrophoresis can be carried out on a dry lipid bilayer membrane, without the membrane being specifically rehydrated. Claim 67 only recites a substrate-supported membrane, and not an electrophoretic process. As disclosed in the written description at, for example, page 8, lines 13-18, such a substrate can be stored in this condition. For subsequent use, the membrane is swelled in water and/or a buffer solution.

In view of the above explanations, it is submitted that the rejection of claims 11, 28, 33, and 45 is ineffective as to claims 57 and 67.

The examiner rejected claims 1, 4, 5, 9, 11, 17, 21-26, 28, 29, 31, 32, 34-39, 41, 43, 44, and 46 as being anticipated by USP 6,228,326 (Boxer et al.).

The rejected claims, which are canceled, correspond to independent claim 47 and the claims that depend from this claim.

Claim 47 recites a method for the electrophoretic separation of particles, particularly of membrane-adherent macromolecules. The method includes applying the particles to be separated on a substrate-supported membrane such that the particles are mobile across a surface of the substrate-supported membrane, and providing an electrical field having a direction that is oriented along the surface across which the particles are mobile. Electrophoresis is performed according to at least one of two different techniques. The first technique requires temporarily modifying the strength and/or the direction of the electrical field such that a resulting force acts on the particles causing

movement among the particles that depends on the length of the particles. The second technique requires using a substrate-supported membrane having a structured surface, wherein the surface of the substrate-supported membrane is structured to provide a force acting on the particles causing movement among the particles that depends on the length of the particles.

In contrast, Boxer et al. disclose arrays of independently-addressable supported fluid bilayer membranes. At column 5, lines 44-49, Boxer et al. disclose a substrate having a surface defining a plurality of distinct bilayer-compatible surface regions separated by one or more bilayer barrier regions. The substrate can be used in a number of different ways, as explained beginning at column 15. In particular, as described beginning at column 19, line 20, the substrate is structured in such a way that the bilayer barrier surface region acts as two-dimensional sieves having progressively smaller openings from one end of the device to the other (see also Fig. 5). At lines 22 and 23, it is disclosed that biomolecules integrated into or attached to the supported bilayer are sorted in this way.

According to the disclosed embodiment (column 19, lines 41-50), membrane-associated molecules are sorted by size by applying a voltage source to cause the charged biomolecules to migrate through the progressively smaller gaps of the consecutive barriers until they get trapped according to size in the well defined on the downstream side by a barrier having gaps too small for the molecules to pass through. According to an alternative embodiment, the bilayer barrier regions are arranged such that the molecules are sorted based on the migration time to the array.

Thus, in contrast to the method of claim 47, the biomolecules sorted by the Boxer et al. array are always part of the supported bilayer, being integrated into or attached to the supported bilayer. According to the first action of the method of claim 47, the particles to be separated are applied **on** a substrate supported membrane such that the particles are mobile **across the surface** of the substrate supported membrane. Thus, this feature of claim 47 is not disclosed by Boxer et al.

Further, Boxer et al. do not disclose temporarily modifying one of the strength and the direction of an electrical field, as recited by claim 47, or its recited alternative of using a substrate-supported membrane having a structured surface. The substrates disclosed by Boxer et al. are treated in such a way as to form bilayer-barrier surfaces so that vesicles in the suspension will not have fused with the surface to form a fluid bilayer (column 6, lines 52-62). The vesicles will either be rinsed off during the rinse step or will remain attached and immobilized on the surface. It is preferred, however, that the vesicles do not stick to the material but can be rinsed off (column 6, lines 62-65).

Therefore, these regions are intended solely to interrupt the membrane at specific parts. This follows also from the term "compartmentalize" used in column 19, line 25. There is no structuring of the membrane surface. An additional indication is also provided in the passage spanning column 22, line 55 to column 23, line 5, where a comparison is made with a surface having a specific topography but without barrier regions. Thus, Boxer et al. explicitly teach that barrier regions are not used. The examiner cited column 19, lines 20-57 as teaching a substrate-supported membrane having a structured surface. However, as pointed out above, the Boxer et al. structure is provided within the supported bilayer, and not on the surface.

For at least the reasons noted above, Boxer et al. do not disclose all of the featured recited in claim 47 and therefore does not anticipate claim 47. Claims 48-61 and 63-66 depend from claim 47 and therefore are also not anticipated by Boxer et al. The rejection, therefore, is ineffective as to claims 48-61 and 63-66.

The examiner rejected claims 35 and 40 as being anticipated by a Biophysical Journal article authored by Groves et al. Claims 35 and 40 are canceled, and no new claims are submitted that correspond to the subject matter of claims 35 and 40.

The examiner rejected claim 2 as being obvious in view of Boxer et al., and further in view of USP 5,637,201 (Raguse et al.).

Claim 2 is canceled. Claim 48 depends from claim 47, and corresponds to the subject matter of canceled claim 2. As noted above, Boxer et al. fail to disclose a number of the features recited in claim 47. For example, Boxer et al. do not disclose particles mobile across a surface of the substrate-supported membrane; temporarily modifying the strength and/or direction of the electrical field; or using a substrate-supported membrane having a structured surface. Raguse et al. also do not disclose these features, and therefore do not overcome the deficiency of Boxer et al. Because neither reference teaches or suggests all of these features, no combination of the teachings of these references could render obvious the invention recited in claim 48. The rejection of claim 2, therefore, is ineffective as to claim 48.

The examiner rejected claim 3 as being obvious in view of Boxer et al. and Raguse et al., and further in view of USP 5,552,155 (Bailey et al.).

Claim 3 is canceled. Claim 49 depends from claim 47, and corresponds to the subject matter of canceled claim 3. As noted above, Boxer et al. and Raguse et al. fail to

disclose a number of the features recited in claim 47. For example, Boxer et al. and Raguse et al. do not disclose particles mobile across a surface of the substrate-supported membrane; temporarily modifying the strength and/or direction of the electrical field; or using a substrate-supported membrane having a structured surface. Bailey et al. also do not disclose these features, and therefore do not overcome the deficiency of Boxer et al. and Raguse et al. Because none of the references teaches or suggests all of these features, no combination of the teachings of these references could render obvious the invention recited in claim 49. The rejection of claim 3, therefore, is ineffective as to claim 49.

The examiner also rejected claims 6-8 as lacking inventive step in view of the Boxer et al. patent, and further in view of EP 0396053 A2 (Allington et al.).

Claims 6-8 are canceled. Claims 52-54 depend from claim 47, and correspond to the subject matter of canceled claims 6-8. As noted above, Boxer et al. fail to disclose a number of the features recited in claim 47. For example, Boxer et al. do not disclose particles mobile across a surface of the substrate-supported membrane; temporarily modifying the strength and/or direction of the electrical field; or using a substrate-supported membrane having a structured surface. Allington et al. also do not disclose these features, and therefore do not overcome the deficiency of Boxer et al. Because neither of the references teaches or suggests all of these features, no combination of the teachings of these references could render obvious the invention recited in claims 52-54. The rejection of claims 6-8, therefore, is ineffective as to claims 52-54.

The examiner rejected claims 10, 13, and 27 as obvious in view of Boxer et al., and further in view of USP 5,427,663 (Austin et al.).

Claims 10, 13, and 27 are canceled. Claims 56 and 59 depend from claim 47, and correspond to the subject matter of canceled claims 10, 13, and 27. As noted above, Boxer et al. fail to disclose a number of the features recited in claim 47. For example, Boxer et al. do not disclose particles mobile across a surface of the substrate-supported membrane; temporarily modifying the strength and/or direction of the electrical field; or using a substrate-supported membrane having a structured surface. Austin et al. also do not disclose these features, and therefore do not overcome the deficiency of Boxer et al. Because neither of the references teaches or suggests all of these features, no combination of the teachings of these references could render obvious the invention recited in claims 56 and 59. The rejection of claims 10, 13, and 27, therefore, is ineffective as to claims 56 and 59.

The examiner rejected claims 12 and 18-20 as obvious in view of Boxer et al., and further in view of USP 6,013,165 (Wiktorowicz et al.).

Claims 12 and 18-20 are canceled. Claims 58 and 64-66 depend from claim 47, and correspond to the subject matter of canceled claims 12 and 18-20. As noted above, Boxer et al. fail to disclose a number of the features recited in claim 47. For example, Boxer et al. do not disclose particles mobile across a surface of the substrate-supported membrane; temporarily modifying the strength and/or direction of the electrical field; or using a substrate-supported membrane having a structured surface. Wiktorowicz et al. also do not disclose these features, and therefore do not overcome the deficiency of Boxer et al. Because neither of the references teaches or suggests all of these features, no combination of the teachings of these references could render obvious the invention

recited in claims 58 and 64-66. The rejection of claims 12 and 18-20, therefore, is ineffective as to claims 58 and 64-66.

The examiner rejected claims 14 and 16 as obvious in view of Boxer et al., and further in view of Groves et al.

Claims 14 and 16 are canceled. Claim 60 depends from claim 47, and corresponds to the subject matter of canceled claim 14. As noted above, Boxer et al. fail to disclose a number of the features recited in claim 47. For example, Boxer et al. do not disclose particles mobile across a surface of the substrate-supported membrane; temporarily modifying the strength and/or direction of the electrical field; or using a substrate-supported membrane having a structured surface. Groves et al. also do not disclose these features, and therefore do not overcome the deficiency of Boxer et al. Because neither of the references teaches or suggests all of these features, no combination of the teachings of these references could render obvious the invention recited in claim 60. The rejection of claim 14, therefore, is ineffective as to claim 60.

Claim 62 is independent, and corresponds to the subject matter of canceled claim 16. Claim 62 recites a method of observing an electrophoretic separation, including applying the particles to be separated on a substrate-supported membrane such that the particles are mobile across a surface of the substrate-supported membrane, and providing an electrical field having a direction that is oriented along the surface across which the particles are mobile. Electrophoresis is performed according to at least one of two different techniques. The first technique requires temporarily modifying the strength and/or the direction of the electrical field such that a resulting force acts on the particles causing movement among the particles that depends on the length of the particles. The

second technique requires using a substrate-supported membrane having a structured surface, wherein the surface of the substrate-supported membrane is structured to provide a force acting on the particles causing movement among the particles that depends on the length of the particles. Digitized image data of the electrophoretic movement is recorded, and the recorded image data is evaluated using a computer.

As noted above, Boxer et al. fail to disclose a number of these features. For example, Boxer et al. do not disclose particles mobile across a surface of the substrate-supported membrane; temporarily modifying the strength and/or direction of the electrical field; or using a substrate-supported membrane having a structured surface. Groves et al. also do not disclose these features, and therefore do not overcome the deficiency of Boxer et al. Because neither of the references teaches or suggests all of these features, no combination of the teachings of these references could render obvious the invention recited in claim 62. The rejection of claim 16, therefore, is ineffective as to claim 62.

The examiner rejected claim 15 as obvious in view of Boxer et al., and further in view of Groves et al. and Raguse et al.

Claim 15 is canceled. Claim 61 depends from claim 47, and corresponds to the subject matter of canceled claim 15. As noted above, Boxer et al., Groves et al., and Raguse et al. all fail to disclose a number of the features recited in claim 47. For example, these references do not disclose particles mobile across a surface of the substrate-supported membrane; temporarily modifying the strength and/or direction of the electrical field; and using a substrate-supported membrane having a structured surface. Because none of the references teaches or suggests all of these features, no

combination of the teachings of these references could render obvious the invention recited in claim 61. The rejection of claim 15, therefore, is ineffective as to claim 61.

The examiner rejected claims 30 and 42 as obvious in view of Boxer et al., and further in view of Bailey et al.

Claims 30 and 42 are canceled. Claims 49 and 50 depend from claim 47, and correspond to the subject matter of canceled claims 30 and 42. As noted above, Boxer et al. fail to disclose a number of the features recited in claim 47. For example, Boxer et al. do not disclose particles mobile across a surface of the substrate-supported membrane; temporarily modifying the strength and/or direction of the electrical field; or using a substrate-supported membrane having a structured surface. Bailey et al. also do not disclose these features, and therefore do not overcome the deficiency of Boxer et al. Because neither of the references teaches or suggests all of these features, no combination of the teachings of these references could render obvious the invention recited in claims 49 and 50. The rejection of claims 30 and 42, therefore, is ineffective as to claims 49 and 50.

Claims 68 and 69 depend from independent claim 67, and correspond to the subject matter of canceled claims 30 and 42. Claim 67 recites a substrate-supported membrane including a substrate and a fluid lipid membrane, wherein the fluid lipid membrane is dried up. As acknowledged by the examiner, Boxer et al. do not disclose or suggest a dried up fluid lipid membrane. It is submitted that Bailey et al. also do not disclose this feature, and therefore do not overcome the deficiency of Boxer et al. Because neither of the references teaches or suggests this feature, no combination of the teachings of these references could render obvious the invention recited in independent

claim 67, and in dependent claims 68 and 69. The rejection of claims 30 and 42, therefore, is ineffective as to claims 68 and 69.

The examiner rejected claims 33 and 45 as obvious in view of Boxer et al., and further in view of USP 5,736,342 (Van Wie et al.).

Claims 33 and 45 are canceled, and correspond most closely to new independent claims 67. Claim 67 recites a substrate-supported membrane including a substrate and a fluid lipid membrane, wherein the fluid lipid membrane is dried up. As acknowledged by the examiner, Boxer et al. do not disclose this.

Van Wie et al. disclose the use of new synthetic lipids and lipid combinations in combination with electrode membrane arrangements. The examiner stated that Van Wie et al. disclose preparation of a lipid bilayer membrane for use in sensors, including a step of drying the membrane, referring to column 10, line 65 through column 11, line 11. It is respectfully submitted that this interpretation of the cited passage is not correct. In the cited passage, it is disclosed that a Kel-F chamber is conditioned by adding a drop of 5% soybean lipid in n-decane. This is allowed to dry. Then, an emulsion with reconstituted receptors is applied so that a bilayer is formed containing the receptors. Therefore, only the soybean lipid is dried, and not the lipid membrane. Thus, a dried lipid membrane is not disclosed by Van Wie et al.

Because neither of the cited references teaches or suggests this feature, no combination of the teachings of these references could render obvious the invention recited in independent claim 67. The rejection of claims 33 and 45, therefore, is ineffective as to claim 67.

In summary, none of the cited references discloses or suggests particles mobile across a surface of the substrate-supported membrane; temporarily modifying the strength and/or direction of the electrical field; using a substrate-supported membrane having a structured surface; or substrate-supported membrane including a substrate and a fluid lipid membrane, wherein the fluid lipid membrane is dried up. Because none of the references discloses or suggests at least these features, no combination of any of the references can render obvious the claimed invention.

Based on the foregoing, it is submitted that all objections and rejections have been overcome. It is therefore requested that the Amendment be entered, the claims allowed, and the case passed to issue.

Respectfully submitted,

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